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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,210	09/28/2005	R Rogers Yocum	BGI-154US	2701

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EXAMINER	
SAIDHA, TEKCHAND	
ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,210	YOCUM ET AL.	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-49* is/are pending in the application.

4a) Of the above claim(s) *1-15 and 28-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 January 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group III, claims 16-27, drawn to a process for enhanced production of pantothenate comprising culturing a microorganism having (i) a deregulated [pantothenate] biosynthetic pathway, (ii) a deregulated isoleucine-valine (ilv) biosynthetic pathway, and (iii) a deregulated methylenetetrahydrofolate (MTF) biosynthetic pathway, under conditions such that pantothenate production is enhanced), in reply filed 7/7/2008, is acknowledged.

In the Restriction Requirement, the Examiner indicates that the special technical feature of Groups I-XV appears to be that they all relate to a process or recombinant organism for producing pantothenate by employing distinct genes or deregulating distinct pathways. As the product pantothenate is known in the art, the Examiner concludes that Groups I-XV share no special technical feature. Applicants respectfully submit that the Examiner has mischaracterized the special technical feature. While the Examiner's understanding of the claimed invention appears to be correct, he appears not to have recognized that the deregulation of specific pathways is claimed, and has provided no more than a mere conclusory statement as to "the art". In particular, Applicants submit that the unifying special technical feature is a process of enhancing production of pantothenate by deregulation of a particular pathway, namely, the methylenetetrahydrofolate (MTF) biosynthetic pathway. This special technical feature is present in at least all of groups I, II, III, VII, VIII, XI, XII, XIII, XIV, and XV. Accordingly, the foregoing groups form a single, unified invention.

Applicants arguments are considered with respect to the product as merely providing a conclusory statement as to the 'art'. This is not found to be persuasive because the product - pantothenic acid or pantothenate is also well known in the art and can be purchased from Sigma. The Sigma product numbers are P2250, P3161 & P9153.

Citing MPEP § 1850. III. A., Applicants argue that-

[t]he method for determining unity of invention under PCT Rule 13 shall be construed as permitting, in particular, the inclusion of any one of the following combinations of claims of different categories in the same international application:

(A) In addition to an independent claim for a given product, an independent claim for a process specially adapted for the manufacture of the said product, and an independent claim for a use of the said product;

(B) In addition to an independent claim for a given process, an independent claim for an apparatus or means specifically designed for carrying out the said process; or

(C) In addition to an independent claim for a given product, an independent claim for a process specially adapted for the manufacture of the said product and an independent claim for an apparatus or means specifically designed for carrying out the said process.

In the instant application, Groups I-III and XI-XV are related to Groups VII and VIII as product and use of said product, i.e., a recombinant microorganism having a deregulated MTF biosynthetic pathway (Groups VII and VIII), and a process for enhanced production of pantothenate comprising culturing said microorganism (Groups I-III and XI-XV). Accordingly, Applicants submit that the restriction between at least Groups I-III, VII-VIII, and Groups XI-XV is improper, and respectfully request that the requirement for restriction among these groups be withdrawn. At a minimum, however, Applicants request that Groups III and VIII be examined together in the instant application, as these groups are related as product and use of said product. In particular, the claims of Group VIII are directed specifically to a recombinant microorganism for enhanced production of pantothenate, said microorganism having a deregulated pantothenate biosynthetic pathway, a deregulated methylenetetrahydrofolate (MTF) biosynthetic pathway, and a deregulated isoleucine-valine (ilv) biosynthetic pathway; while the claims of Group III are directed to a process for enhanced production of pantothenate, comprising culturing a microorganism having said features. Accordingly, Applicants request that the requirement for restriction among the foregoing groups be reconsidered and withdrawn.

Applicants' arguments are considered and not found to be persuasive because the various methods comprise distinct method steps, are therefore distinct inventions.

The lack of unity determination is still deemed proper and is therefore made FINAL.

2. Claims 16-27 are under consideration in this examination.

3. **Claims withdrawn** :

Claims 1-15 & 28-49 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed.

4. ***Specification***

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25-27 recite the limitation "wherein CoaA.....CoaX; or CoaX...CoaA; or CoaX and CoaA" in claim 24. There is insufficient antecedent basis for this limitation in the claim. Claims 25-27 are rejected for lack of antecedent basis.

6. Claim Rejections - 35 USC § 112 (first paragraph)

Enablement

Claims 16-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for enhanced production of pantothenate (pantothenic acid) comprising culturing a strain of *Bacillus* transformed with a plasmid pAN396 (figure 6, SEQ ID NO: 24) over expressing (deregulated) serine hydroxymethyl transferase (the *glyA* gene product); or culturing a strain of *Bacillus* transformed with a plasmid pAN393 (Figure 7, SEQ ID NO: 25) over expressing (deregulated) 3-phosphoglycerate dehydrogenase (the *SerA* gene product), **does not** reasonably provide enablement for a process for enhanced production of pantothenate, comprising culturing any microorganism having (i) a deregulated [pantothenate] biosynthetic pathway, (ii) a deregulated isoleucine-valine (ilv) biosynthetic pathway, and (iii) a deregulated methylenetetrahydrofolate (MTF) biosynthetic pathway, under conditions such that pantothenate production is enhanced, wherein one to several enzymes are deregulated, optionally comprising pantothenate kinase activity (Claims 16-27).

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims. Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988))[*Ex parte* Forman [230 USPQ 546 (Bd. Pat. App. & Int. 1986)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim. The factors most relevant to this rejection are [the scope of the claims, unpredictability in the art, the amount of direction or guidance presented, and the amount of experimentation necessary].

The specification, however, only exemplifies 2 specific plasmid constructs, i.e., plasmid pAN396 & pAN393 (*see* specification, examples III & IV) for increased production of pantothenate, as an alternate to serine feeding. These expression cassettes are functional only in *B. subtillis* (*see* instant specification, page 38, lines 1-7). There is no disclosure or description of other members of the methylenetetrahydrofolate (MFT) biosynthetic pathway or pantothenate biosynthetic pathway genes from any source. The specification does not teach the specific structure of *glyA and SerA* genes from any biological source.

The standard of meeting enablement requirement is whether one of skill in the art can make the invention without undue experimentation. The amount of experimentation to make the claimed invention is enormous and undue. Such experimentation entails or involves isolating and deregulating enormous number of (i) [pantothenate] biosynthetic pathway genes, (ii) isoleucine-valine (ilv) biosynthetic pathway genes, and (iii) methylenetetrahydrofolate (MTF) biosynthetic pathway genes, all from any source under conditions such that pantothenate production is enhanced. This would involve isolating and optimizing numerous plasmid constructs, and transforming any host cell or microorganism for over expression (or deregulation) and enhanced pantothenate production; which is well outside the realm of routine experimentation and predictability

in the art of success is extremely high given the lack of guidance or information is provided regarding the extremely large number genes involved in the preparation of specific plasmid constructs and host microorganisms. It would be nearly impossible for one skilled in the art to extrapolate the 2 examples to include the enormous number of (i) [pantothenate] biosynthetic pathway genes, (ii) isoleucine-valine (ilv) biosynthetic pathway genes, and (iii) methylenetetrahydrofolate (MTF) biosynthetic pathway genes.

The Examiner finds that one skilled in the art would require additional guidance regarding gene sequences involved in the pathways from any source or at least a representative number of sequences, plasmid and microbial constructs that can effectively increase pantothenate production. Without such guidance, the experimentation left to those skilled in the art is undue.

7. ***Written Description***

Claims 16-27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 16-27 are directed to a process for enhanced production of pantothenate, comprising culturing any microorganism having (i) a deregulated [pantothenate] biosynthetic pathway, (ii) a deregulated isoleucine-valine (ilv) biosynthetic pathway, and (iii) a deregulated methylenetetrahydrofolate (MTF) biosynthetic pathway, under conditions such that pantothenate production is enhanced, wherein one to several enzymes are deregulated, optionally comprising pantothenate kinase activity (Claims 16-27). The method involves a genus of genes of the various pathways required in the production of pantothenate.

The specification provides description of *two species* to the process for enhanced production of pantothenate (pantothenic acid) comprising culturing a strain of *Bacillus* transformed with a plasmid pAN396 (figure 6, SEQ ID NO: 24) over expressing (deregulated) serine hydroxymethyl transferase (the *glyA* gene product); or culturing a strain of *Bacillus* transformed with a plasmid pAN393 (Figure 7, SEQ ID NO: 25) over expressing (deregulated) 3-phosphoglycerate dehydrogenase (the *SerA* gene product).

The specification discloses structural information of the DNA sequence of SEQ ID No. 24 and SEQ ID NO: 25 involved in the two specific plasmid constructs (species) required in the process for enhancing pantothenate of the claimed genus of numerous plasmid constructs involving a vast number of genes required for the process claimed which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. The 2 species disclosed are not representative of the genus of genes used in the process of enhanced pantothenate production.

According to MPEP 2163, to satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba, B.V. v.Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed.Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116.

The method steps reciting the products must comply with the written description requirement. The claims are genus claims directed toward a method using a genus of genes deregulated in the various biosynthetic pathways (see above) for enhanced production of pantothenate.

The scope of each genus includes many members of (i) [pantothenate] biosynthetic pathway genes, (ii) isoleucine-valine (ilv) biosynthetic pathway genes, and (iii) methylenetetrahydrofolate (MTF) biosynthetic pathway genes encoding enzymes with widely differing structural, chemical, and physical characteristics. Furthermore, each genus is highly variable because a significant number of structural differences between genus members exits. Recitation of the name of the "biosynthetic pathway or names of the genes" and its source as a "specific microorganism" do not define any structural features such as nucleic acid or amino acid sequences commonly possessed by the genus. The specification does not describe and define any structural features and/or nucleic acid or amino acid sequences commonly possessed by each genus. There is no art-recognized correlation between any structure of a pathway genes (or the encoding enzyme) and any "biosynthetic pathways". Those of ordinary skill in the art

would not be able to identify without further testing what specific "biosynthetic pathways genes or enzyme' are being involved that can be used in the claimed method.

MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification fails to disclose additional genes/enzyme that are involved in the biosynthetic pathways, and therefore in the method for the enhanced production pantothenate. As such the disclosure of the above 2 minimal examples are insufficient to be representative of the attributes and features common to all the members of each claimed genus. Thus, one skilled in the art cannot visualize or recognize the identity of the members of each claimed genus.

In view of the above considerations, one of skill in the art would not recognize that applicants were in possession of the invention recited in claims 16-27, at the time the instant application was filed.

8. ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 16-27 rejected under the judicially created doctrine of double patenting over claims 1-34 of U. S. Patent No.7,244,593 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows:

The instant claims 16-27 are directed to a process for enhanced production of pantothenate, comprising culturing any microorganism having (i) a deregulated [pantothenate] biosynthetic pathway, (ii) a deregulated isoleucine-valine (ilv) biosynthetic pathway, and (iii) a deregulated methylenetetrahydrofolate (MTF) biosynthetic pathway, under conditions such that pantothenate production is enhanced, wherein one to several enzymes are deregulated, optionally comprising pantothenate kinase activity (Claims 16-27), broad genus claims. The patent claims (Patent No.7,244,593) are drawn to a method for enhanced production of pantothenate comprising culturing a microorganism having MTF biosynthetic enzymes encoded by over-expression of specific *Bacillus glyA* and/or *Bacillus sera* genes, species claims. Claims 7 onwards recite further involvement of specific genes of the (ii) a deregulated isoleucine-valine (ilv) biosynthetic pathway, and (iii) a deregulated methylenetetrahydrofolate (MTF) biosynthetic pathway. The patented species claims therefore anticipates the instantly claimed genus claims.

Claims 16-27 are provisionally rejected under the judicially created doctrine of double patenting over claims 15-21, 36 & 37-40 of copending Application No. **11/879,143**. This is a provisional double patenting rejection since the conflicting claims have not yet been patented. Election is due in this case at the time of writing the Office Action. The claims appear identical in scope and are therefore anticipated.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha whose telephone number is (571) 272 0940. The examiner can normally be reached on 8.30 am - 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed can be reached on (571) 272 0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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